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Activated 10/1/58

TOBACCO INDUSTRY RESEARCH COMMITTEE
150 East Forty Second Street
New York 17, N. Y.

Application for Research Grant

Date: June 8, 1959

1. Name of Investigator: Sydney C. Rittenberg
2. Title: Professor of Bacteriology
3. Institution & Address: Department of Bacteriology
University of Southern California
Los Angeles 7, California
4. Project or Subject: The bacterial degradation of nicotine and related compounds. The goal of the project is the elucidation of the intermediary metabolism of nicotine oxidation.
5. Detailed Plan of Procedure: The program and progress of this investigation have been detailed in past grant applications, in semi-annual and annual reports, and in the two papers published to date. On the assumption that the above material is part of the record, only a brief statement of the work contemplated for next year is included here.

It is our intent to continue the research along the lines of the past three years. The identification of the third oxidative product, which we now have in crystalline form, is currently receiving most attention. We have recently worked out the conditions necessary for the accumulation of the fourth product and a chromatographic technique for its detection. We will shortly attempt a large scale (several hundred milligrams) enzymatic synthesis of this compound and start purification and identification studies as was done for the three preceding metabolic intermediates. We will investigate the conditions necessary for the accumulation of the fifth oxidative product. Since our enzyme preparations oxidize nicotine beyond this point, and since the chromatographic technique worked out for the fourth compound may also apply to the fifth, the prerequisites for this phase of the work are completed.

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Finally, over the course of last year we have obtained, by isolation and from other investigators, a collection of about a dozen different nicotine oxidizing bacteria. We plan to investigate the ability of these organisms to metabolize the intermediates of nicotine oxidation we have isolated using the simultaneous adaptation technique. From such studies we should get some information as to whether the pathway of nicotine oxidation carried out by our organism is a general one. It is improbable that more than the above, if that much, will be completed within the next year.

6. Budget Plan:	Salaries	\$4,800.00
	Expendable Supplies	1,500.00
	Permanent Equipment	
	Overhead	532.00
	Other = Travel	350.00
	Total	\$7,182.00

7. Anticipated Duration of Work: One year for work outlined. About two additional years to complete the project.

8. Facilities and Staff Available: The facilities of a well equipped bacteriology-biochemistry laboratory are available and no additional needs are anticipated.

The staff will consist of the director of the project and two graduate students. One, Mr. S. Richardson, has advanced to candidacy for the Ph.D. degree and will be working essentially full time on the project. He will receive \$3600 for the year. The second student, not yet chosen, will be working only part-time, and will be used mainly to assist in organic syntheses and other chemical aspects of the program.

9. Additional Requirements: None.

10. Additional Information (Including relation of work to other projects and other sources of supply):

The relation of our work to projects in progress elsewhere and to current knowledge of nicotine metabolism has been discussed in previous grant applications and in the semi-annual and annual reports, and there is little new to mention here.

University of Southern California
University Park
Los Angeles 7, California

Signature /s/ Sydney C. Rittenberg
Director of Project

/s/ Elton D. Phillips
Business Officer of the Institution

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